

REMARKS

In addition to the required elections and selections, the Examiner has seemingly combined an action on the merits by stating that the invention of Group I is anticipated by WO 02/00232. Applicant respectfully traverses this apparent finding and states that WO 02/00232 does not anticipate claim 32.

Claim 32 of the present application is directed to *Bacillus* spores expressing a genetic construct that encodes a therapeutically active compound and further comprising either a signal sequence or a vegetative cell gene. The vegetative cell gene can encode a vegetative cell protein or the rRNA of the *rrnO* gene.

In contrast, WO 02/00232 is concerned with recombinant spores that display chosen proteins fused to spore coat proteins. The genes encoding such spore coat proteins are expressed only during sporulation, and the proteins produced are only displayed on the surface of a spore. Therefore, such genes are *not* expressed when a *Bacillus* cell is in a vegetative state. Such genes are not vegetative cell genes as specified by claim 32. Vegetative cell genes are only expressed in a vegetative cell, that is, a cell which has germinated from the spore state, and do not encompass spore proteins.

Similarly, signal sequences direct transport of a protein to a particular cellular location, or for secretion or for post-translational modification. Such activities cannot be performed by a spore, therefore the use of signal sequences is clearly distinct from the use of spore coat genes.

Thus, in WO 02/00232 the gene employed encodes a spore coat protein fused to the protein of choice and does not encode a signal sequence or a vegetative cell protein or rRNA as specified by claim 32. The subject matter of claim 32 is not anticipated by WO 02/00232.

Furthermore, the spores specified by claim 32 and methods of treatment employing them, as specified by claim 75, are non-obvious over WO 02/00232.

WO 02/00232 is concerned with delivering a compound fused to a spore coat protein. This approach is consistent with what was known in the art at the time of filing of the present application. Since *Bacillus* are naturally soil-dwelling bacteria, the skilled person would not have expected that significant numbers of *Bacillus* spores would germinate into vegetative cells in the gastro-intestinal tract (GIT).

The skilled person would therefore have continued to use spore coat proteins and would not have considered the use of genes whose expression is dependent on spore germination, such as the vegetative cell genes and signal sequences specified by claim 32.

The skilled person would therefore have assumed that vegetative cell gene expression would not be sufficiently high to produce useful amounts of any therapeutic agent delivered in association with such a gene. Similarly, since few spores would be expected to germinate, it would not be expected that association of a therapeutic agent with a signal sequence would result in delivery of effective amounts of said agent.

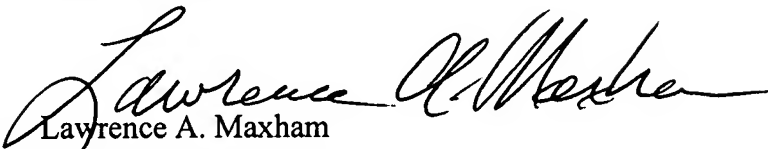
The skilled person would have been led away from the use of vegetative cell genes and signal sequences as a reliable means for expressing a therapeutically active protein in the GIT. Instead, the skilled person would have focussed their efforts on the use of spore coat proteins as taught by WO 02/00232 and would not have considered the use of vegetative cell genes or signal sequences as a viable option.

CONCLUSION

It is believed that Applicant has responded to all issues raised by the Examiner and an action on the merits is requested.

Respectfully submitted,

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